

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

**Amendment**

**In the Claims**

1. (currently amended) An orally administerable abuse-deterring pharmaceutical composition comprising a therapeutically effective amount of a drug prone to abuse selected from the group of compositions consisting of

(a) a composition comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse, and

(b) a water-insoluble, preferably lipophilic, formulation comprising a therapeutically effective amount of a drug prone to abuse materials selected from the group consisting of fats, fatty substances, waxes, wax-like substances and mixtures thereof,

Wherein the drug is dispersed within the water-insoluble formulation, and prevents the immediate release of a portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to an aqueous medium.

2. (currently amended) The An orally administerable abuse-deterring pharmaceutical composition of claim 1 comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse dispersed within a carrier material which is either slowly soluble in water or insoluble in water.

3. (original) The composition of Claim 1, wherein the composition is a controlled-release pharmaceutical composition.

4. (currently amended) The composition of claim 2 +, wherein the drug is dispersed within the water-insoluble formulation, and prevents the immediate release of a

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substantial portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to an aqueous or non-aqueous medium.

5. (currently amended) The composition of Claim 4, wherein the portion of the drug released immediately is less than 80% of the total amount of drug incorporated into formulation.

6. (currently amended) The composition of Claim 4 †, wherein the composition prevents the immediate release of a substantial portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to an aqueous medium, wherein the formulation comprises materials selected from the group consisting of fats, fatty substances, waxes, wax-like substances and mixtures thereof.

7. (original) The composition of Claim 6, wherein the portion of the drug released immediately is less than 80% of the total amount of the drug incorporated into the composition.

8. (original) The composition of Claim 1 wherein the drug prone to abuse is selected from the group consisting of 1-phenylcyclohexylamine, 1-piperidinocyclohexanecarbonitrile, alfentanil, alphacetylmethadol, alphaprodine, alprazolam, amobarbital, amphetamine, anileridine, apomorphine, aprobarbital, barbital, barbituric acid derivative, bemidone, benzoylegonine, benzphetamine, betacetylmethadol, betaprodine, bezitramide, bromazepam, buprenorphine, butabarbital, butalbital, butorphanol, camazepam, cathine, chloral, chlordiazepoxide, clobazam, clonazepam, clorazepate, clotiazepam, cloxazolam, cocaine, codeine, chlorphentermine,

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delorazepam, dexfenfluramine, dextromoramide, dextropropoxyphen, dezocine,  
diazepam, diethylpropion, difenoxin, dihydrocodeine, dihydromorphone, dioxaphentyl  
butyrate, dipanone, diphenoxylate, diprenorphine, econidine, enadoline, eptazocine,  
estazolam, ethoheptazine, ethyl lofazepate, ethylmorphine, etorphine, fempropone,  
fencamfamin, fenfluramine, fentanyl, fludiazepam, flunitrazepam, flurazepam,  
glutethimide, halazepam, haloxazolam, hexalgon, hydrocodone, hydromorphone,  
isomethadone, hydrocodone, ketamine, ketazolam, ketobemidone, levanone,  
levoalphacetylmethadol, levomethadone, levomethadyl acetate, levomethorphan,  
levorphanol, lofentanil, loperamide, loprazolam, lorazepam, lormetazepam, lysergic acid,  
lysergic acid amide, mazindol, medazepam, mesenorex, meperidine, meptazinol,  
metazocine, methadone, methamphetamine, methohexital, methotrimeprazine,  
methyldihydromorphinone, methylphenidate, methylphenobarbital, metopon, morphine,  
nabilone, nalbuphine, nalbupine, nalorphine, narceine, nefopam, nicomorphine,  
nimetazepam, nitrazepam, nordiazepam, normethadone, normorphine, oxazepam,  
oxazolam, oxycodone, oxymorphone, pentazocine, pentobarbital, phenadoxone,  
phenazocine, phencyclidine, phendimetrazine, phenmetrazine, pheneridine, piminodine,  
prodilidine, properidine, propoxyphene, racemethorphan, racemorphan, racemoramide,  
remifentanil, secobarbital, sufentanil, talbutal, thebaine, thiamylal, thiopental, tramadol,  
trimeperidine, vinbarbital, allobarbitone, alprazolam, amylobarbitone, aprobarbital,  
barbital, barbitone, benzphetamine, brallobarbital, bromazepam, brotizolam, buspirone,  
butalbital, butobarbitone, butorphanol, camazepam, captodiame, carbromal, carfentanil,  
carpipramine, cathine, chloral, chloral betaine, chloral hydrate, chloralose,  
chlor diazepoxide, chlorhexadol, chlormethiazole edisylate, chlormezanone, cinolazepam,

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clobazam, potassium clorazepate, clotiazepam, cloxazolam, cyclobarbitone, delorazepam, dexfenfluramine, diazepam, diethylpropion, difebarbamate, difenoxin, enciprazine, estazolam, ethyl loflazepate, etizolam, febarbamate, fencamfamin, fenfluramine, fenproporex, fluanisone, fludiazepam, flunitraam, flunitrazepam, flurazepam, flutoprazepam, gepirone, glutethimide, halazepam, haloxazolam, hexobarbitone, ibomal, ipsapirone, ketazolam, loprazolam mesylate, lorazepam, lormetazepam, mazindol, mebutamate, medazepam, mefenorex, mephobarbital, meprobamate, metaclazepam, methaqualone, methohexital, methylpentynol, methylphenobarbital, midazolam, milazolam, morphine, nimetazepam, nitrazepam, nordiazepam, oxazepam, oxazolam, paraldehyde, pemoline, pentobarbitone, pentazocine, pentobarbital, phencyclidine, phenobarbital, phenidimetrazine, phenmetrazine, phenprobamate, phentermine, phenyacetone, pinazepam, pipradol, prazepam, proxibarbal, quazepam, quinalbaritone, secobarbital, secbutobarbitone, sibutramine, temazepam, tetrazepam, triazolam, triclofos, zalepan, zaleplon, zolazepam, zolpidem, and zopiclone.

9. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a free base or a free acid of the drug.

10. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a salt comprising the ionized drug and a lipophilic counter-ion.

11. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a complex comprising one or more components selected from the group consisting of drug molecules, metal cations, and lipophilic counter-ions.

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12. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a complex comprising one or more components selected from the group consisting of drug molecules, metal cations, and cyclodextrin molecules.

13. (original) The composition of Claim 2 wherein the drug is complexed with a metal cation selected from the group consisting of zinc, calcium, magnesium, bismuth and combinations thereof.

14. (canceled)

15. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is a complex comprising the drug and a cyclodextrin.

16. (original) The composition of Claim 2, wherein the lipophilic derivative of a drug is an ester or amide formed between the drug and a fatty acid.

17. (original) The composition of Claim 4 2, wherein the drug is incorporated into a plurality of individual microparticles comprising a material that is either slowly soluble in water or water insoluble.

18. (original) The composition of Claim 17 wherein the microparticles comprise a wax or wax-like material.

19. (original) The composition of Claim 17 wherein the microparticles comprise a fat or a fatty substance.

20. (original) The composition of Claim 17 wherein the microparticles comprise a material selected from the group consisting of naturally water insoluble proteins, naturally water insoluble polysaccharides, naturally water insoluble lipids and phospholipids, cross-linked water soluble proteins, cross-linked water soluble polysaccharides, cross-linked water soluble cyclodextrins and combinations thereof.

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21. (original) The composition of Claim 17 wherein the individual microparticles are coated with one or more independent layers, where at least one of the layers is water insoluble and is degraded by enzymes of the human gastrointestinal tract.

22. (original) The composition of Claim 1 wherein the drug is in the form of individual drug particles coated with one or more independent layers where at least one of the layers is water insoluble and is degraded by enzymes of the human gastrointestinal tract.

23. (original) The composition of Claim 21 wherein at least one of the layers is water-insoluble, organic solvent-insoluble, and degradable by enzymes present in the human gastrointestinal tract.

24. (original) The composition of Claim 21 comprising materials wherein a combination of these materials is not soluble in water, organic solvent, or any combination thereof.

25. (original) The composition of Claim 21 wherein the composition is not completely soluble, and

wherein the drug is not fully released in a single solvent or enzyme solution.

26. (original) The composition of Claim 21 wherein the enzymatically degradable layer(s) comprise a material selected from the group consisting of naturally water insoluble proteins, naturally water insoluble polysaccharides, naturally water insoluble lipids and phospholipids, cross-linked proteins, cross-linked polysaccharides, and combinations thereof.

27. (original) The composition of Claim 1 wherein the drug prone to abuse is co-administered with a drug that has no appreciable abuse potential.

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28. (original) The composition of claim 1 formulated for the drug to be immediately released upon oral administration.

29. (original) The composition of claim 1 wherein the drug prone to abuse is oxycodone.

30-32. (canceled)

33. (new) The composition of Claim 2 wherein the drug prone to abuse is a lipophilic derivative of a drug selected from the group consisting of 1-phenylcyclohexylamine, 1-piperidinocyclohexanecarbonitrile, alfentanil, alphacetylmethadol, alphaprodine, alprazolam, amobarbital, amphetamine, anileridine, apomorphine, aprobarbital, barbital, barbituric acid derivative, bemicodone, benzoylcegonine, benzphetamine, betacetylmethadol, betaprodine, bezitramide, bromazepam, buprenorphine, butabarbital, butalbital, butorphanol, camazepam, cathine, chloral, chlordiazepoxide, clobazam, clonazepam, clorazepate, clotiazepam, cloxazolam, cocaine, codeine, chlorphentermine, delorazepam, dexfenfluramine, dextromoramide, dextropropoxyphen, dezocine, diazepam, diethylpropion, difenoxin, dihydrocodeine, dihydromorphone, dioxaphenyl butyrate, dipanone, diphenoxylate, diprenorphine, ecgonine, enadoline, eptazocine, estazolam, ethoheptazine, ethyl lofazepate, ethylmorphine, etorphine, fentanyl, fencamfamin, fenfluramine, fentanyl, fludiazepam, flunitrazepam, flurazepam, glutethimide, halazepam, haloxazolam, hexagonal, hydrocodone, hydromorphone, isomethadone, hydrocodone, ketamine, ketazolam, ketobemidone, levanone, levoalphacetylmethadol, levomethadone, levomethadyl acetate, levomethorphan, levorphanol, lofentanil, loperamide, loprazolam, lorazepam, lormetazepam, lysergic acid, lysergic acid amide, mazindol, medazepam,

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mefenorex, meperidine, meptazinol, metazocine, methadone, methamphetamine, methohexital, methotriimeprazine, methylidihydromorphinone, methylphenidate, methylphenobarbital, metopon, morphine, nabilone, nalbuphine, nalbupine, nalorphine, narceine, nefopam, nicomorphine, nimetazepam, nitrazepam, nordiazepam, normethadone, normorphine, oxazepam, oxazolam, oxycodone, oxymorphone, pentazocine, pentobarbital, phenadoxone, phenazocine, phencyclidine, phendimetrazine, phenmetrazine, pheneridine, piminodine, prodilidine, properidine, propoxyphene, racemethorphan, racemorphan, racemoramide, remifentanil, secobarbital, sufentanil, talbutal, thebaine, thiamylal, thiopental, tramadol, trimeperidine, vinbarbital, allobarbitone, alprazolam, amylobarbitone, aprobarbital, barbital, barbitone, benzphetamine, brallobarbital, bromazepam, brotizolam, buspirone, butalbital, butobarbitone, butorphanol, camazepam, captodiame, carbromal, carfentanil, carpipramine, cathine, chloral, chloral betaine, chloral hydrate, chloralose, chlordiazepoxide, chlorhexadol, chlormethiazole edisylate, chlormezanone, cinolazepam, clobazam, potassium clorazepate, clotiazepam, cloxazolam, cyclobarbitone, delorazepam, dexfenfluramine, diazepam, diethylpropion, difebarbamate, difenoxin, enciprazine, estazolam, ethyl loflazepate, etizolam, febarbamate, fencamfamin, fenfluramine, fenproporex, fluanisone, fludiazepam, flunitraam, flunitrazepam, flurazepam, flutoprazepam, gepirone, glutethimide, halazepam, haloxazolam, hexobarbitone, ibomal, ipsapirone, ketazolam, loprazolam mesylate, lorazepam, lormetazepam, mazindol, mebutamate, medazepam, mefenorex, mephobarbital, meprobamate, metaclazepam, methaqualone, methohexital, methylpentynol, methylphenobarbital, midazolam, milazolam, morphine, nimetazepam, nitrazepam,

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nordiazepam, oxazepam, oxazolam, paraldehyde, pemoline, pentobarbitone, pentazocine, pentobarbital, phencyclidine, phenobarbital, phenemetrazine, phenmetrazine, phenprobamate, phentermine, phenyacetone, pinazepam, pipradol, prazepam, proxibarbal, quazepam, quinalbaritone, secobarbital, secbutobarbitone, sibutramine, temazepam, tetrazepam, triazolam, triclofos, zalepan, zaleplon, zolazepam, zolpidem, and zopiclone.

34. (new) The composition of Claim 2 wherein the lipophilic derivative is dissolved in the carrier material in a molten state to result in a uniform dispersion within the carrier material.

35. (new) The composition of Claim 2 wherein the lipophilic derivative is dissolved in a co-solvent along with a carrier material to result in a uniform dispersion within the carrier material.

36. (new) The composition of Claim 10 wherein the lipophilic counter-ion is selected from the group consisting of stearic acid, palmitic acid, and mixtures thereof.

37. (new) The composition of Claim 1 comprising one or more excipients selected from the group consisting of stearic acid, palmitic acid, and mixtures thereof.

38. (new) The composition of Claim 1 comprising one or more excipients selected from the group consisting of beeswax, carnauba wax, hydrogenated oil, and mixtures thereof.